

### IN THE CLAIMS

Please cancel non-elected claims 1-16, 18-31, 41, and 47-52, without prejudice.  
Please add the new claims 53 and 54. The following listing of claims replaces all prior listings.

1-16 (Canceled).

17. (Currently amended) A method for analyzing ~~determining in~~ a plurality of proteomic mixtures ~~the presence of active target members of a group of related proteins in each of said proteomic mixtures, said related proteins related in having a common functionality for conjugation at an active site,~~ said method comprising:

(a) combining each of said ~~proteomic~~ mixtures with at least one activity-based probe, wherein:

(a1) each mixture includes a group of related proteins, the group comprising active target members;

(a2) said probe(s) includes a functionality allowing conjugation of said probe to said target members,

whereby said probe(s) is conjugated to said target member comprising a reactive functionality specific for said active site when active, under conditions for conjugation of said probe(s) to said target members to form an adduct; and

(b) determining the presence of said target members conjugated with said probe adduct in each of said ~~proteomic~~ mixtures;  
whereby the presence of said ~~target members conjugated to said probe(s) adduct~~ in said ~~proteomic~~ mixtures is indicative of the presence of active target members in said mixtures, wherein said related proteins include a common functionality for conjugation at an active site.

18-31. (Canceled)

32. (Currently amended). A method according to Claim 17 or 53 ~~48~~, additionally comprising ~~the additional step of~~ characterizing said active target members conjugated with said probe(s).

33. (Previously presented). A method according to Claim 32, wherein said characterizing comprises degrading said active target member and determining the resulting fractions by mass spectrometry.

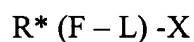
34. (Currently amended). A method according to Claim 17 or 53 ~~48~~, employing a plurality of activity-based probes having different reactive functionalities specific for different groups of related proteins.

35. (Currently amended). A method according to Claim 17 or 53 ~~48~~, wherein said activity-based probe(s) comprises a detectable label.

36. (Currently amended). A method according to Claim 17 or 53 ~~48~~, wherein said proteomic mixture is in an intact cell.

37. (Currently amended). A method according to Claim 17 or 53 ~~48~~, further comprising ~~the step of~~ analyzing for the presence of proteins conjugated with said probe(s) using simultaneous individual capillary electrokinetic analysis or capillary HPLC.

38. (Currently amended) A method according to Claim ~~44~~, 17, ~~48 or 49~~ wherein said activity-based probe(s) are of the formula:



wherein:

X is a ligand for binding to a reciprocal receptor or a chemically reactive functionality for reacting with a reciprocal functionality to add a ligand;

L is a linking group;

F is a functional group reactive at an active site of a target enzyme; and

R is H or a moiety of less than 1kDal providing specific affinity for said target enzymes;

the \* intends that R is a part of F or L.

39. (Previously presented). A method according to Claim 38, wherein F is a sulphonyl group and R is other than H and bonded to F.

40. (Previously presented). A method according to Claim 38, wherein F is a fluorophosphonyl or fluorophosphoryl group.

41. (Canceled).

42. (Currently amended) A method according to any of Claims ~~11-13, 15-21~~, 32, 33, 35-38, or 40, ~~or 41~~ wherein said activity-based probe(s) are fluorophosphonate-biotin (FP-biotin).

43. (Currently amended) A method according to any of Claims ~~11-13, 15-21~~, 32, 33, 35-38, or 40, ~~or 41~~ wherein said activity-based probe(s) are FP-peg-biotin.

44. (Currently amended) A method according to any of Claims ~~11-13, 15-20, 23, 24~~ 17, 32, 33, 35-39 or 53-~~41~~ wherein said activity-based probe(s) are selected from the group consisting of 10-((2-pyridylsulfonyl)oxo)-N-biotinamidopentyldecanamide, 10-((Benzenesulfonyl)oxo)-N-biotinamidopentyldecanamide, 10-((*p*-Toluenesulfonyl)oxo)-N-biotinamidopentyldecanamide, 10-((4-Methoxybenzenesulfonyl)oxo)-N-biotinamidopentyldecanamide, 10-((Methylsulfonyl)oxo)-N-

biotinamidopentyldecanamide, 10-((Butylsulfonyl)oxo)-*N*-  
biontinamidopentyldecanamide, 10-((Octylsulfonyl)oxo)-*N*-  
biotinamidopentyldecanamide, 10-((4-Nitrobenzenesulfonyl)oxo)-*N*-  
biotinamidopentyldecanamide, 10-((8-Quinolinesulfonyl)oxo)-*N*-  
biotinamidopentyldecanamide, 10-((2-Naphthalenesulfonyl)oxo)-*N*-  
biotinamidopentyldecanamide, 10-((2-Thiophenesulfonyl)oxo)-*N*-  
biotinamidopentyl)decanamide,  $\alpha$ -undecylenyl alcohol, ((2-pyridylsulfonyl)oxo)-10-  
undecene, 10-((2-pyridylsulfonyl)oxo)-decanoic acid, 1-(2-pyridylsulfonyl)oxo-octane,  
1-(2-pyridylsulfonyl)oxo-ethane, and 1-(methanesulfonyl)oxo-octane.

45. (Previously presented) A method according to claim 44 wherein said activity-based probe is 1-(2-pyridylsulfonyl)oxo-octane.

46. (Currently amended) A method according to Claim ~~14~~ or 34 wherein said activity-based probe(s) are selected from the group consisting of FP-biotin, FP-peg-biotin, 10-((2-pyridylsulfonyl)oxo)-*N*-biotinamidopentyldecanamide, 10-((Benzenesulfonyl)oxo)-*N*-biotinamidopentyldecanamide, 10-((*p*-Toluenesulfonyl)oxo)-*N*-biotinamidopentyldecanamide, 10-((4-Methoxybenzenesulfonyl)oxo)-*N*-biotinamidopentyldecanamide, 10-((Methylsulfonyl)oxo)-*N*-biotinamidopentyldecanamide, 10-((Butylsulfonyl)oxo)-*N*-biontinamidopentyldecanamide, 10-((Octylsulfonyl)oxo)-*N*-biotinamidopentyldecanamide, 10-((4-Nitrobenzenesulfonyl)oxo)-*N*-biotinamidopentyldecanamide, 10-((8-Quinolinesulfonyl)oxo)-*N*-biotinamidopentyldecanamide, 10-((2-Naphthalenesulfonyl)oxo)-*N*-biotinamidopentyldecanamide, 10-((2-Thiophenesulfonyl)oxo)-*N*-biotinamidopentyl)decanamide,  $\alpha$ -undecylenyl alcohol, ((2-pyridylsulfonyl)oxo)-10-undecene, 10-((2-pyridylsulfonyl)oxo)-decanoic acid, 1-(2-pyridylsulfonyl)oxo-octane, 1-(2-pyridylsulfonyl)oxo-ethane, and 1-(methanesulfonyl)oxo-octane.

47-52. (Canceled).

53. (New) A method for determining in a plurality of proteomic mixtures the presence of active target members of a group of related proteins in each of said proteomic mixtures, said related proteins related in having a common functionality for conjugation at an active site, said method comprising:

combining each of said proteomic mixtures with at least one activity-based probe comprising a reactive functionality specific for said active site when active, under conditions for conjugation of said probe(s) to said target members;

determining the presence of target members conjugated with said probe in each of said proteomic mixtures;

whereby the presence of said target members conjugated to said probe(s) in said proteomic mixtures is indicative of the presence of active target members in said mixtures,

wherein said activity-based probe(s) have the formula:

$R^* (F - L) - X$

wherein:

X is a ligand for binding to a reciprocal receptor or a chemically reactive functionality for reacting with a reciprocal functionality to add a ligand;

L is a linking group;

F is a functional group reactive at an active site of a target enzyme; and

R is H or a moiety of less than 1kDal providing specific affinity for said target enzymes;

the \* intends that R is a part of F or L.

54. (New) A method for screening for the bioactivity of a candidate compound toward a group of related target proteins in a proteomic mixture of proteins from a cell, employing at least one probe, each probe characterized by comprising a reactive

functionality group specific for said group of target proteins and a ligand and said probe, said method comprising:

- (a) combining at least one probe with an untreated portion of said mixture and with a portion inactivated with a non-covalent agent under conditions for reaction with said target proteins;
- (b) sequestering proteins conjugated with said at least one probe from each of said mixtures;
- (c) determining the proteins that are sequestered; and
- (d) comparing the amount of each of the proteins sequestered from the untreated portion and the inactivated portion as indicative of the bioactivity of said candidate compound with said target proteins.